Dementia

Definition

Progressive irreversible deterioration of higher cognitive function in clear consciousness. Must involve at least two cognitive domains

- Memory
- Language
- Visuospatial function
- Praxis
- Gnosis
- Frontal: planning, social skills, verbal fluency, motor sequencing, abstract thinking

Mild cognitive impairment (MCI) = impairment of memory with preservation of other cognitive domains and intact activities of daily living (30% develop dementia within 2y)

Aetiology

Common

- Alzheimer's disease 50%
- Vascular dementia 20-30%

- Lewy body dementia 20%
- Alcoholic dementia 10%

Rare

- Irreversible
  - Trauma (dementia pugilistica)
  - Infection: HIV, HSV encephalitis, neurosyphilis, CJD
  - Degenerative: Parkinson's, Huntington's, Pick's
  - Demyelinating: MS
- Potentially reversible
  - Metabolic: hypothyroidism; vitamin B1/B12/folate deficiency
  - Hydrocephalus: actual or normal pressure
  - Space-occupying lesions: subdural haematoma, neoplasm (frontal)
  - Depression (pseudodementia)

Management

Pharmacological management options are very limited at present.

Alzheimer's disease (AD)

Cholinesterase inhibitors (AChE-Is)

Neuronal degeneration in AD goes along with reduced levels of many neurotransmitters, but post-mortem studies show a characteristic degeneration of cholinergic neurones in the basal forebrain nuclei. In animal experiments, lesions of the nucleus basalis produce cognitive and learning deficits.

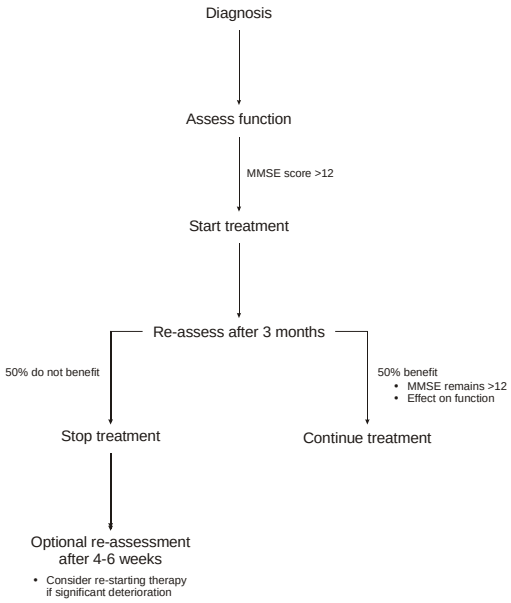
AChE-Is have been shown to provide some cognitive enhancement in patients with Alzheimer's disease. However, a recent review concluded that "because of flawed methods and small clinical benefits, the scientific basis for recommendations of cholinesterase inhibitors for the treatment of Alzheimer's is questionable."[1]

Agents used in AD differ from their cousins used in anaesthesia in their ability to cross the blood-brain barrier. They can act at the anionic site, the esteratic site or both.

While drugs may slow cognitive decline, they do not alter disease progression. Rapid deterioration may occur on withdrawal.

[1] KADUSZKIEWICZ, H. ET AL. (2005): Cholinesterase inhibitors for patients with Alzheimer's disease: a systematic review of randomised controlled trials. *BMJ* **331**:321-3.

Who should be treated?
NICE has approved the use of donepezil/rivastigmine/galantamine in mild to moderate Alzheimer's provided that the following algorithm is followed *in a specialist clinic*:



Side-effects
Cholinergic: N/V/D, bradycardia, heart block, cramps, convulsions, urinary incontinence

Donepezil
- Reversible inhibitor at anionic site
- Once daily dosing
- Well tolerated

Rivastigmine
- 'Pseudo-irreversible' inhibitor at anionic and esteratic site
- Given twice daily PO, or by transdermal patch
- No liver metabolism and low protein binding → safe in liver disease and few drug interactions

Galantamine
- Reversible inhibitor
- Given twice daily
- Additional presynaptic nicotinic agonist action → ?increased ACh release

Other strategies
Memantine
NMDA-receptor antagonist that affects glutamate transmission, licensed for treating moderate to severe Alzheimer's disease.

Nicotinic agonists

Amyloid-beta peptide vaccination
- Experimental treatment but very promising
- Reduces amyloid deposition and memory deficits in transgenic mice
- Human trials to follow

Antioxidants
E.g. vitamin E, selegiline, Ginko

Glial cell modulators
Propentofylline prevents inflammatory response, not specific to AD

Vascular dementia
Modification of cardiovascular risk factors

Co-medication
- Eliminate or reduce unnecessary drugs
- Benzodiazepines: can cause disinhibition and should be avoided
- Antipsychotics: as required, but beware in Parkinson's and Lewy body dementia (can cause severe extra-pyramidal features)
- Antidepressants: SSRIs are less likely to cause confusion than TCAs